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[0087] Two standard polymerase chain reactions were carried out using the Hir_insf1/Insu11HindIII primer pair with plasmid pINT90d as template and the pfuf1/Hir_insrev primer pair with plasmid pBpfu_hir as template. To perform the reactions the ~~Advantage~~ADVANTAGE™-HF PCR Kit (Clontech Cat#K1909-1) was used. The reaction volume was 50 µl containing 1 µl polymerase, 5-10 ng template and about 100 ng of primer. 25 cycles: 30" at 95° C., 30" at 52° C. and 30" at 72° C. were run. The products of both reactions were isolated and about 5% of the yields were combined and converted in a third polymerase chain reaction which was run under the same conditions with primers pfuf1/Insu11HindIII. The result was a DNA product which contained the sequence signal (partially)-lepirudin-GNSAR-simian proinsulin. The DNA fragment was converted using restriction enzymes BamHI and HindIII (according to the manufacturer's protocol), with BamHI cleaving in the lepirudin sequence and HindIII at the 3' end of the proinsulin-encoding sequence.

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[0100] The peptide sequence was translated into DNA by the GCG program Backtranslate (~~Wisconsin Package~~WISCONSIN PACKAGE™ Version 10.1, Genetics Computer Group (GCG), Madison, Wis.) using the E. coli high codon usage criteria.

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[0111] The hirudin concentration of the supernatant of Example 5 was determined according to the method of Grießbach et al. (Thrombosis Research 37, pp. 347-350 1985, which is incorporated by reference herein in its entirety). For this purpose, ~~Refludan~~REFLUDAN™ standard was included in the measurements in order to establish a calibration curve from which the yield in mg/l was determined directly. The biological activity (unfolded molecules are not active) was also a direct measure for correct folding of the proinsulin component of the fusion protein. Alternatively, although not conducted as part of this Example, it is possible to use a proteolytic Staphylococcus aureus digestion and subsequent analysis in an RP-HPLC system in order to perform a peptide mapping to determine the correct S-S bridge formation.

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Amendments to the Specification

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Please amend paragraph ***[0129]*** *as follows:*

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[0129] Signal sequence ecoompc derived from *E. coli* ompC gene coding for major outer membrane protein (~~GenEMBL data base locus: SMOMPA, 1364 bp, DNA BCT Mar. 20 1995~~).

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